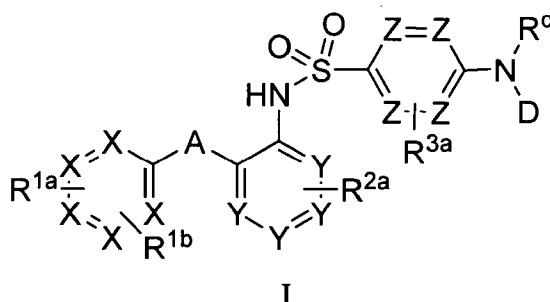


Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. **(currently amended)** A compound of formula I and pharmaceutically acceptable salts thereof:



wherein

A is O, CO, S, NR<sup>d</sup>, or CR<sup>b</sup>R<sup>c</sup>;

D is COR<sup>4</sup>, C(O)NR<sup>d</sup>R<sup>4</sup>, C(O)OR<sup>4</sup>, SO<sub>2</sub>R<sup>4</sup>, SO<sub>2</sub>NR<sup>d</sup>R<sup>4</sup>;

X, Y and Z are independently a ring carbon atom or a ring nitrogen atom, with the proviso that 0-3 X, 0-3 Y and 0-3 Z are ring nitrogen atoms;

R<sup>1a</sup> and R<sup>1b</sup> are independently selected from (1) H, (2) halogen, (3) C<sub>1-6</sub>alkyl optionally substituted with 1-5 groups independently selected from halogen, nitro, cyano, COR<sup>a</sup>, CO<sub>2</sub>R<sup>a</sup>, C(O)NR<sup>d</sup>Re, OR<sup>a</sup>, OC(O)R<sup>a</sup>, SR<sup>a</sup>, SO<sub>2</sub>R<sup>f</sup>, S(O)R<sup>f</sup>, NR<sup>d</sup>Re, NR<sup>d</sup>C(O)R<sup>a</sup> and NR<sup>d</sup>SO<sub>2</sub>R<sup>f</sup>, (4) C(O)R<sup>a</sup>, (5) CO<sub>2</sub>R<sup>a</sup>, (6) C(O)NR<sup>d</sup>Re, (7) OR<sup>a</sup>, (8) OC(O)R<sup>a</sup>, (9) OC(O)NR<sup>d</sup>Re, (10) NR<sup>d</sup>Re, (11) NR<sup>d</sup>C(O)R<sup>a</sup>, (12) NR<sup>d</sup>C(O)OR<sup>a</sup>, (13) NR<sup>d</sup>C(O)NR<sup>d</sup>Re, (14) NR<sup>d</sup>SO<sub>2</sub>R<sup>f</sup>, (15) SR<sup>a</sup>, (16) S(O)R<sup>f</sup>, (17) SO<sub>2</sub>R<sup>f</sup>, (18) SO<sub>2</sub>NR<sup>d</sup>Re, (19) CN, (20) NO<sub>2</sub>, (21) optionally substituted aryl, (22) optionally substituted heteroaryl, (23) optionally substituted heterocyclyl, (24) optionally substituted aryl-C<sub>1-6</sub>alkyl, (25) optionally substituted heteroaryl-C<sub>1-6</sub>alkyl, and (26) optionally substituted heterocyclyl-C<sub>1-6</sub>alkyl; wherein the substituents for aryl, heteroaryl, heterocyclyl, aralkyl, heteroaralkyl and heterocyclylalkyl are 1 to 3 groups independently selected from halogen, cyano, nitro, OR<sup>a</sup>, NR<sup>d</sup>Re, NR<sup>d</sup>C(O)R<sup>a</sup>, NR<sup>d</sup>SO<sub>2</sub>R<sup>f</sup>, OC(O)R<sup>a</sup>, NR<sup>d</sup>C(O)<sub>2</sub>R<sup>a</sup>, SR<sup>a</sup>,

Serial No.: 10/561,319  
Case No.: Case 21444YP  
Page No.: 5

SO<sub>2</sub>R<sup>f</sup>, oxo (for heterocyclyl and heterocyclylalkyl), C(O)R<sup>a</sup>, C(O)<sub>2</sub>R<sup>a</sup>, C<sub>1-4</sub> alkyloxy, aryl, aryl-C<sub>1-4</sub>alkyl, heteroaryl, heteroaryl-C<sub>1-4</sub>alkyl, C<sub>3-6</sub> cycloalkyl and C<sub>1-4</sub> alkyl optionally substituted with 1 to 5 halogen atoms, or

R<sup>1a</sup>, R<sup>1b</sup> and adjacent carbon atoms to which they are attached together form a saturated, partially unsaturated or aromatic 5- or 6-membered ring containing 0 to 2 heteroatoms selected from N, N-R<sup>g</sup>, O and S;

R<sup>2a</sup> and R<sup>3a</sup> are independently selected from (1) H, (2) halogen, (3) OR<sup>a</sup>, (4) NR<sup>d</sup>Re, (5) CN, (6) NO<sub>2</sub>, (7) CO<sub>2</sub>R<sup>a</sup>, (8) COR<sup>a</sup>, and (9) C<sub>1-4</sub> alkyl optionally substituted with 1 to 5 halogen atoms,

R<sup>4</sup> is selected from (1) C<sub>1-6</sub>alkyl substituted with 1 to 5 halogen atoms, OR<sup>a</sup>, NR<sup>d</sup>Re or C(O)NR<sup>d</sup>Re in which, for these two occurrences, R<sup>d</sup> and R<sup>e</sup> together complete a 4- to 8-membered ring optionally containing an additional heteroatom selected from NR<sup>g</sup>, O, S, and SO<sub>2</sub>, and said ring being optionally fused to a benzene or a 5- or 6-membered heteraromatic ring, and optionally substituted with 1 to 3 substituents independently selected from halogen, cyano, nitro, OR<sup>g</sup>, oxo, C<sub>3-6</sub> cycloalkyl, aryl, heteroaryl, NR<sup>g</sup>R<sup>g</sup>, NR<sup>g</sup>COR<sup>g</sup>, NR<sup>g</sup>CO<sub>2</sub>R<sup>g</sup> and C<sub>1-4</sub> alkyl optionally substituted with 1 to 5 halogen atoms; (2) optionally substituted heteroaryl; (3) optionally substituted heteroaryl-C<sub>1-4</sub>alkyl; (4) optionally substituted heterocyclyl; (4)<sup>5</sup> optionally substituted heterocyclyl-C<sub>1-4</sub>alkyl; wherein the substituents for heteroaryl, heteroaralkyl, heterocyclyl and heterocyclylalkyl are 1 to 3 groups independently selected from halogen, cyano, nitro, OR<sup>a</sup>, NR<sup>d</sup>Re, NR<sup>d</sup>C(O)R<sup>a</sup>, NR<sup>d</sup>SO<sub>2</sub>R<sup>f</sup>, OC(O)R<sup>a</sup>, NR<sup>d</sup>C(O)<sub>2</sub>R<sup>a</sup>, SR<sup>a</sup>, SO<sub>2</sub>R<sup>f</sup>, oxo (for heterocyclyl and heterocyclylalkyl), C(O)R<sup>a</sup>, C(O)<sub>2</sub>R<sup>a</sup>, C<sub>1-4</sub> alkyloxy, aryl, aryl-C<sub>1-4</sub>alkyl, heteroaryl, heteroaryl-C<sub>1-4</sub>alkyl, C<sub>3-6</sub> cycloalkyl and C<sub>1-4</sub> alkyl optionally substituted with 1 to 5 halogen atoms (1) H, (2) C<sub>1-6</sub>alkyl optionally substituted with 1 to 5 groups independently selected from halogen, nitro, cyano, C<sub>3-6</sub>cycloalkyl, COR<sup>a</sup>, CO<sub>2</sub>R<sup>a</sup>, C(O)NR<sup>d</sup>Re, OR<sup>a</sup>, OC(O)R<sup>a</sup>, SR<sup>a</sup>, SO<sub>2</sub>R<sup>f</sup>, S(O)R<sup>f</sup>, NR<sup>d</sup>Re, NR<sup>d</sup>C(O)R<sup>a</sup>, NR<sup>d</sup>SO<sub>2</sub>R<sup>f</sup>, and NR<sup>d</sup>C(O)<sub>2</sub>R<sup>a</sup>, (3) optionally substituted C<sub>3-6</sub>cycloalkyl, (4) COR<sup>a</sup>, (5) COOR<sup>a</sup>, (6) optionally substituted aryl, (7) optionally substituted heteroaryl, (8) optionally substituted heterocyclyl, (9) optionally substituted aryl-C<sub>1-6</sub>alkyl, (10) optionally substituted heteroaryl-C<sub>1-6</sub>alkyl, and (11) optionally substituted heterocyclyl-C<sub>1-6</sub>alkyl; wherein the substituents for cycloalkyl, aryl, heteroaryl, heterocyclyl, aralkyl, heteroaralkyl and heterocyclylalkyl are 1 to 3 groups independently selected from halogen, cyano, nitro, OR<sup>a</sup>, NR<sup>d</sup>Re, NR<sup>d</sup>C(O)R<sup>a</sup>, NR<sup>d</sup>SO<sub>2</sub>R<sup>f</sup>, OC(O)R<sup>a</sup>, NR<sup>d</sup>C(O)<sub>2</sub>R<sup>a</sup>, SR<sup>a</sup>, SO<sub>2</sub>R<sup>f</sup>, oxo (for heterocyclyl and heterocyclylalkyl), C(O)R<sup>a</sup>, C(O)<sub>2</sub>R<sup>a</sup>, C<sub>1-4</sub> alkyloxy, aryl

~~optionally substituted with 1 or 2 halogen atoms, aryl-C<sub>1-4</sub>alkyl, heteroaryl, heteroaryl-C<sub>1-4</sub>alkyl, C<sub>3-6</sub>cycloalkyl and C<sub>1-4</sub>alkyl optionally substituted with 1 to 5 halogen atoms;~~

~~R<sup>4'</sup> is a group selected from R<sup>4</sup> except R<sup>4'</sup> is not H; ———~~

R<sup>a</sup> is (1) H, (2) C<sub>1-6</sub> alkyl optionally substituted with 1 to 5 groups independently selected from halogen, cyano, nitro, OH, C<sub>1-4</sub> alkyloxy and C<sub>3-6</sub> cycloalkyl, (3) C<sub>3-6</sub> cycloalkyl, (4)

optionally substituted aryl, (5) optionally substituted heteroaryl, (6) optionally substituted heterocyclyl, (7) optionally substituted aryl-C<sub>1-6</sub>alkyl, (8) optionally substituted heteroaryl-C<sub>1-6</sub>alkyl, and (9) optionally substituted heterocyclyl-C<sub>1-6</sub>alkyl; wherein the substituents for aryl,

heteroaryl, heterocyclyl, aralkyl, heteroaralkyl and heterocyclylalkyl are 1 to 3 groups independently selected from halogen, cyano, nitro, OR<sup>g</sup>, NR<sup>d</sup>Re, NR<sup>d</sup>C(O)R<sup>g</sup>, NR<sup>d</sup>SO<sub>2</sub>R<sup>f</sup>, OC(O)R<sup>g</sup>, NR<sup>d</sup>C(O)<sub>2</sub>R<sup>g</sup>, SR<sup>g</sup>, SO<sub>2</sub>R<sup>f</sup>, oxo (for heterocyclyl and heterocyclylalkyl), C(O)R<sup>g</sup><sub>a</sub>, C(O)<sub>2</sub>R<sup>g</sup>, C<sub>1-4</sub> alkyloxy, aryl, aryl-C<sub>1-4</sub>alkyl, heteroaryl, heteroaryl-C<sub>1-4</sub>alkyl, C<sub>3-6</sub> cycloalkyl and C<sub>1-4</sub> alkyl optionally substituted with 1 to 5 halogen atoms;

R<sup>b</sup> and R<sup>c</sup> are independently selected from H, halogen, or C<sub>1-4</sub>alkyl optionally substituted with 1 to 5 halogen atoms;

R<sup>d</sup> and R<sup>e</sup> are independently selected from (1) H, (2) C<sub>1-4</sub>alkyl, optionally substituted with 1 to 5 groups independently selected from halogen, amino, mono-C<sub>1-4</sub>alkylamino, di-

C<sub>1-4</sub>alkylamino, and SO<sub>2</sub>R<sup>f</sup>, (3) aryl-C<sub>1-6</sub>alkyl optionally substituted with 1 to 3 groups selected from halogen, cyano, nitro, OH, C<sub>1-4</sub> alkyloxy, C<sub>3-6</sub> cycloalkyl and C<sub>1-4</sub> alkyl optionally substituted with 1 to 5 halogen atoms, (4) heteroaryl-C<sub>1-6</sub>alkyl optionally substituted with 1 to 3 groups selected from halogen, cyano, nitro, OH, C<sub>1-4</sub> alkyloxy, C<sub>3-6</sub> cycloalkyl and C<sub>1-4</sub> alkyl optionally substituted with 1 to 5 halogen atoms, and (5) C<sub>3-6</sub> cycloalkyl, or

R<sup>d</sup> and R<sup>e</sup>, or R<sup>d</sup> and R<sup>4</sup>, ~~or R<sup>d</sup> and R<sup>4'</sup>~~, together with the atom or atoms to which they are attached, complete a 4- to 8-membered saturated, partially saturated or aromatic ring optionally containing 1 to 3 heteroatoms independently selected from N, NR<sup>g</sup>, O, S, and SO<sub>2</sub>, and said ring being optionally fused to a benzene or a 5- or 6-membered heteraromatic ring, and optionally substituted with 1 to 3 substituents independently selected from halogen, cyano, nitro, OR<sup>g</sup>, oxo, C<sub>3-6</sub> cycloalkyl, aryl, aryl-C<sub>1-4</sub>alkyl, heteroaryl, NR<sup>g</sup>R<sup>g</sup>, NR<sup>g</sup>COR<sup>g</sup>, NR<sup>g</sup>CO<sub>2</sub>R<sup>g</sup> and C<sub>1-4</sub> alkyl optionally substituted with 1 to 5 halogen atoms;

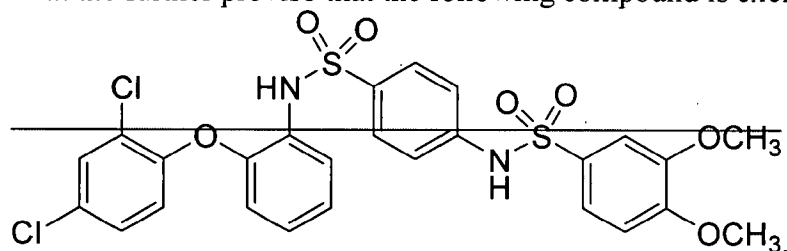
R<sup>f</sup> is selected from (1) C<sub>1-4</sub> alkyl optionally substituted with 1 to 5 halogen atoms, (2) C<sub>1-4</sub> alkyloxy, and (3) aryl optionally substituted with 1 to 3 groups selected from halogen, cyano,

nitro, OH, C<sub>1-4</sub> alkyloxy, C<sub>3-6</sub> cycloalkyl and C<sub>1-4</sub> alkyl optionally substituted with 1 to 5 halogen atoms;

R<sub>g</sub> is selected from (1) H, (2) C<sub>1-4</sub>alkyl, (3) aryl, (4) aryl-C<sub>1-6</sub>alkyl, (5) C(O)<sub>2</sub>C<sub>1-4</sub>alkyl and (6) C(O)C<sub>1-4</sub>alkyl;

~~with the proviso that when each occurrence of X, Y and Z is a ring carbon atom, R<sup>1a</sup> and R<sup>1b</sup> are each hydrogen or chlorine, and R<sup>2a</sup> and R<sup>2b</sup> are each hydrogen, then D is not NHC(O)C<sub>1-6</sub>alkyl;~~

~~with the further proviso that the following compound is excluded:~~



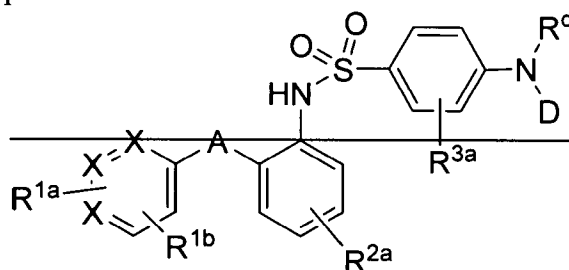
2. **(original)** A compound of Claim 1 wherein A is C(O) or O.

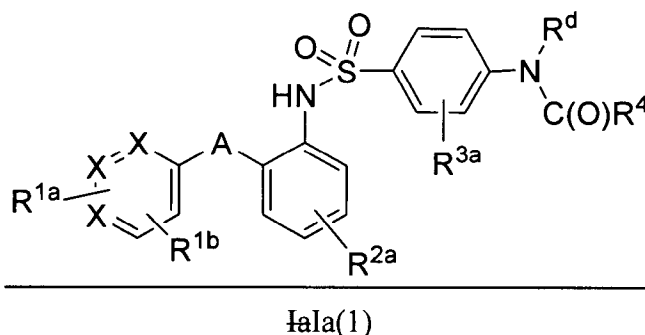
3. **(canceled)**

4. **(original)** A compound of Claim 1 wherein each occurrence of Y and Z represents a ring carbon atom, and one X is a ring carbon or nitrogen atom and the others are ring carbon atoms.

5. **(canceled)**

6. **(currently amended)** A compound of Claim 1 having the formula Ia(1) and pharmaceutically acceptable salts thereof:





wherein

A is O or C(O);

one of X is a ring carbon or nitrogen atom, and the others are ring carbon atoms;

D is C(O)R<sup>4</sup>, C(O)NR<sup>d</sup>R<sup>4</sup> or C(O)OR<sup>4</sup>;

R<sup>1a</sup> and R<sup>1b</sup> are independently selected from hydrogen, halogen, C<sub>1-4</sub>alkyl, cyano, SR<sup>a</sup>, OR<sup>a</sup> and CF<sub>3</sub>;

R<sup>2a</sup> and R<sup>3a</sup> are independently H or halogen;

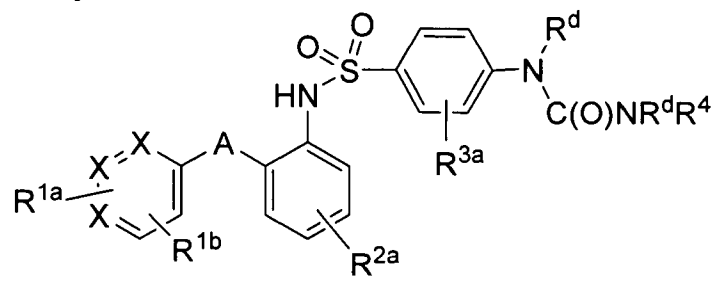
R<sup>4</sup> is selected from (1) C<sub>1-4</sub>alkyl substituted with one to 5 groups independently selected from halogen, C<sub>3-6</sub> cycloalkyl, NR<sup>d</sup>Re, NR<sup>d</sup>C(O)OR<sup>a</sup>, C(O)NR<sup>d</sup>Re, C(O)OR<sup>a</sup>, and OR<sup>a</sup>; (2) C<sub>3-6</sub>cycloalkyl; (3) phenyl; (4) phenyl-C<sub>1-4</sub>alkyl; (5) optionally substituted heteroaryl; (6) optionally substituted heteroaryl-C<sub>1-4</sub>alkyl; (7) optionally substituted heterocyclyl; and (8) optionally substituted heterocyclyl-C<sub>1-4</sub>alkyl; wherein heteroaryl, including as part of heteroarylalkyl, is selected from benzofuranyl, pyrazolo[1,5-a]pyrimidinyl, 1-azaindoliziny, s-triazolo[1,5-a]pyrimidinyl, thieno[3,2-b]pyridinyl, isoxazolyl, pyrazinyl, pyrazolyl, pyrimidinyl, benzisoxazolyl, pyridyl, indolyl, benzimidazolyl, benzthiazolyl and imidazo[2,1-b]thiazolyl; heterocyclyl, including as part of heterocyclylalkyl, is selected from morpholinyl, tetrahydropyranyl, tetrahydrofuranyl, pyrrolidinyl, piperidinyl and imidazolidinyl; the substituents for heteroaryl is 1 or 2 groups independently selected from C<sub>1-4</sub>alkyl, C<sub>3-6</sub>cycloalkyl, and OR<sup>a</sup>; and the substituents for heterocyclyl is 1 to 3 groups independently selected from oxo and C<sub>1-4</sub>alkyl,

R<sup>a</sup> and R<sup>d</sup> are as defined in Claim 1.

7. (canceled)

8. **(currently amended)** A compound of Claim 7-6 wherein  $R^4$  is selected from (1)  $C_1$ -4alkyl substituted with  $NR^dR^e$  or  $C(O)NR^dR^e$  where for both groups  $R^d$  and  $R^e$ , together with the nitrogen atom to which they are attached, complete an optionally substituted 5- or 6-membered saturated ring having 0 to 1 additional ring heteroatom selected from NRG, O, S and  $SO_2$ , and wherein said substituent is 1 or 2 groups independently selected from  $OR^a$ , halogen,  $C_1$ -4alkyl and oxo; (2) optionally substituted heteroaryl wherein said heteroaryl is selected from pyrazolyl, isoxazolyl, pyrimidinyl, benzofuranyl, pyrazolo[1,5-a]pyrimidinyl, 1-azaindoliziny, s-triazolo[1,5-a]pyrimidinyl, imidazo[2,1-b]thiazolyl, thieno[3,2-b]pyridinyl, and said substituent is 1 to 3 groups independently selected from furanyl, pyridyl, benzyl, phenyl optionally substituted with halogen,  $C_1$ -4alkyl,  $C_3$ -6cycloalkyl, trifluoromethyl, halogen, and  $C_1$ -4alkoxy.

9. **(currently amended)** A compound of Claim 6-1 having the formula Ia(2) and pharmaceutically acceptable salts thereof:



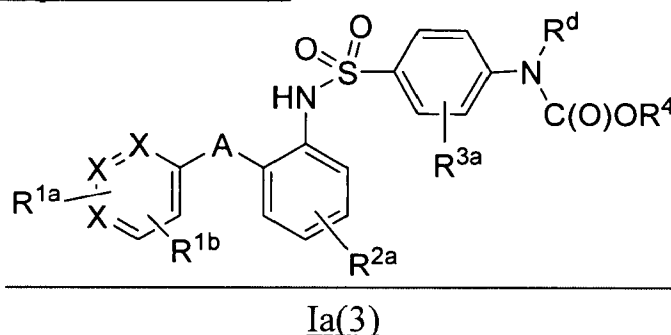
Ia(2)

wherein  $D$  is  $C(O)NR^dR^4$ , wherein  $R^d$  is H and  $R^4$  is selected from (1)  $C_1$ -4alkyl substituted with a group selected from halogen,  $OR^a$ ,  $CO_2R^a$ ,  $NHCOR^a$ ,  $NR^dR^e$  and  $C(O)NR^dR^e$ ; (2) optionally substituted heteroaryl- $C_1$ -4alkyl wherein heteroaryl is selected from azaindoliziny, imidazolyl, imidazolyl, benzimidazolyl, pyrazinyl, pyridyl, indolyl, triazolyl, thiazolyl, imidazo[1,2-a]pyridyl, imidazo[1,2-a]pyrimidinyl, imidazo[2,1-b]thiazolyl, and pyrazolo[1,5-a]pyrimidinyl; (3) optionally substituted heterocyclyl- $C_1$ -4alkyl wherein heterocyclyl is selected from tetrahydropyranyl, tetrahydrofuranyl and dioxanyl; (4) optionally substituted heterocyclyl selected from pyrrolidinyl and piperidinyl; (5)  $CO_2R^a$ ; (6)  $C_3$ -6cycloalkyl; and (7) optionally substituted phenyl- $C_1$ -4alkyl; or  $R^d$  and  $R^4$  together with the nitrogen atom to which they are attached complete an optionally substituted 5- or 6-membered saturated ring having 0 to 1 additional ring heteroatom selected from NRG, O, S and  $SO_2$ , wherein said ring is optionally

fused to a benzene or a 5- or 6-membered heteroaryl ring, and said substituent is 1 or 2 groups independently selected from OR<sup>a</sup>, halogen, C<sub>1-4</sub>alkyl, NR<sup>d</sup>Re, NR<sup>d</sup>CO<sub>2</sub>R<sup>a</sup>, and oxo.

10. **(original)** A compound of Claim 9 wherein R<sup>d</sup> is H and R<sup>4</sup> is selected from (1) C<sub>1-4</sub>alkyl substituted with NR<sup>d</sup>Re or C(O)NR<sup>d</sup>Re, wherein for both groups R<sup>d</sup> and Re together with the nitrogen to which they are attached complete an optionally substituted 5- or 6-membered saturated ring having 0 to 1 additional ring heteroatom selected from NR<sup>g</sup>, O, S and SO<sub>2</sub>, and wherein said substituent is 1 or 2 groups independently selected from OR<sup>a</sup>, halogen, C<sub>1-4</sub>alkyl and oxo; (2) heterocyclyl or heterocyclyl-C<sub>1-4</sub>alkyl wherein said heterocyclyl is selected from pyrrolidinyl, 1,4-dioxanyl, and tetrahydropyranyl; and (3) heteroaryl-C<sub>1-4</sub>alkyl optionally substituted with 1 to 3 C<sub>1-4</sub>alkyl groups, wherein said heteroaryl is selected from imidazolyl, 1-azaindoliziny, imidazo[2,1-b]thiazolyl, and pyrimidinyl.

11. **(currently amended)** A compound of Claim 7-1 having the formula Ia(3) an pharmaceutically acceptable salts thereof:



wherein ~~D~~ is C(O)OR<sup>4</sup>, and R<sup>4</sup> is selected from (1) C<sub>2-4</sub>alkyl substituted with NR<sup>d</sup>Re or C(O)NR<sup>d</sup>Re in which, for these two groups, R<sup>d</sup> and Re together with the nitrogen atom to which they are attached complete an optionally substituted 5- or 6-membered saturated ring having 0 to 1 additional ring heteroatom selected from NR<sup>g</sup>, O, S and SO<sub>2</sub>, and wherein said substituent is 1 or 2 groups independently selected from OR<sup>a</sup>, halogen, C<sub>1-4</sub>alkyl and oxo; (2) heterocyclyl-C<sub>1-4</sub>alkyl optionally substituted with 1 to 3 groups independently selected from C<sub>1-4</sub>alkyl and oxo, wherein heterocyclyl is selected from tetrahydropyranyl, tetrahydrofuranyl, pyrrolidinyl, morpholinyl, oxazolidinyl, dioxanyl, and dioxolanyl; (3) furanyl-C<sub>1-4</sub>alkyl; and (4) phenyl-C<sub>1-4</sub>alkyl.

Serial No.: 10/561,319  
Case No.: Case 21444YP  
Page No.: 11

12. **(canceled)**

13. **(original)** A pharmaceutical composition comprising a therapeutically effective amount of a compound of formula I, or a pharmaceutically acceptable salt thereof, and pharmaceutically acceptable excipients.

14. **(currently amended)** ~~Use of a compound of formula I or a pharmaceutically acceptable salt thereof in the manufacture of a medicament useful in~~ A method for the treatment or prevention of diseases or disorders mediated through the bradykinin receptor pathway which comprises administering to a patient in need thereof a compound of formula I or a pharmaceutically acceptable salt thereof.

15. **(currently amended)** The ~~use~~ method of Claim 14 wherein said disease or disorder is selected from neuropathic pain, acute pain and inflammatory pain.